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Alcohol Consumption and Marijuana Use Interaction with Metabolic Syndrome among United States Adults: Analysis of NHANES 2013-2014.

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ABSTRACT

ALCOHOL CONSUMPTION AND MARIJUANA USE INTERACTION WITH METABOLIC SYNDROME AMONG UNITED STATES ADULTS: ANALYSIS OF NHANES 2013-2014.

By

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INTRODUCTION: The relationship between alcohol, marijuana and metabolic syndrome remains controversial. Marijuana has been found to be a commonly used drug among those who drink alcohol, yet little is known about the effect of using both substances concurrently with metabolic syndrome. With decriminalization of marijuana across different states in the United States, it is expected that the prevalence of marijuana use will increase. Therefore, it is of utmost importance to understand the adverse impact of these drugs on metabolic syndrome.

AIM: This study aims to understand (a) the relationship between alcohol and marijuana use and metabolic syndrome (b) the association between concurrent use of alcohol and marijuana and metabolic syndrome, and (c) the statistical interaction of alcohol and marijuana use on metabolic syndrome using the National Health and Nutrition Examination Survey data.

METHODS: A cross-sectional analysis of 2013-2014 National Health and Nutrition Examination survey data was conducted. Participants aged ≥20 years were eligible. Metabolic syndrome was defined by the International Diabetes Federation criteria. The adjusted odds ratio of metabolic syndrome was calculated controlling for variables fitted using stepwise logistic regression model selection.

RESULTS: After adjusting for age, race, educational level, marital status, poverty, and cigarette smoking status; current drinkers showed a significant inverse association with metabolic syndrome (aOR, 0.69 95% CI, 0.49-0.99). The odds of metabolic syndrome in concurrent users (aOR 0.53 95% CI, 0.28-0.99) was less than the odds among non-concurrent users. Compared with young adults, middle-aged and older adults had increased odds of metabolic syndrome.

DISCUSSION: This data indicates that alcohol consumption and co-use of alcohol and marijuana is associated with a lower prevalence of metabolic syndrome. Longitudinal studies are needed to confirm these findings. Notably, age and smoking are significant predictors of metabolic syndrome.

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Author's Statement Page

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CHAPTER I – INTRODUCTION

1.1. Background

Cardiovascular diseases are the leading cause of death both worldwide and in the United States.[1,2] The risk factors for these diseases tend to aggregate in individuals, and the collective presence of three or more of these factors has been referred to as Insulin resistance syndrome or Syndrome X or Metabolic syndrome.

Metabolic syndrome is a disease entity characterized by central obesity, impaired fasting glucose, raised blood pressure, raised triglycerides and reduced high-density lipoprotein (HDL) cholesterol.[3] It is a heterogeneous cardiovascular risk factor, in that each element of this syndrome can be a risk factor independently. Research by Stern, William & Gonzalez-Villalpando (as cited in IDF consensus statement, 2006) concluded that about a quarter of the world's adult population has metabolic syndrome.[4] Compared to people without the syndrome, those with metabolic syndrome are twice as likely to die from and thrice more likely to have a heart attack or stroke.[2] Metabolic syndrome poses an indirect economic burden worldwide in that it increases the risk of Type 2 diabetes by fivefold. The annual direct health care cost attributed to diabetes worldwide is around 289 billion international dollars (ID), and it is estimated the cost will increase to over 300 billion ID by 2025. Addressing this problem is therefore of prime concern. Aside the significant risk factors for metabolic syndrome, other factors implicated include sedentary lifestyle, use of substances such as cigarette, alcohol, and marijuana.

Alcohol consumption and illicit drug use, including marijuana among adults Americans is a widespread and incessant public health problem with colossal physical, social and economic consequences for the nation. In 2015, about 13.6 million adults and 22.2 million aged 12 years and older were current users of marijuana and alcohol respectively.[4] The role of alcohol and marijuana and its effect on metabolic syndrome remain controversial. Studies suggest that alcohol consumption is related to metabolic syndrome. Light to moderate consumption of alcohol has been found to inversely related with metabolic syndrome, while heavy consumption is associated with an increased risk of metabolic syndrome by influencing its components.[5]

Marijuana remains a commonly used illicit drug among those who drink.[6] The swift evolution of marijuana policies over the years highlights the need to understand the interaction of these two drugs and its adverse metabolic outcomes.[7] Past research on the association of marijuana on metabolic syndrome has revealed conflicting results.[8,9] Numerous relationships between independent use of alcohol and marijuana, and risk of metabolic syndrome has been established, there remains a gap in research about the effect of co-use of both drugs on metabolic syndrome. Also, there have been very little research on the interaction of alcohol and marijuana use on metabolic syndrome.

1.2 Research Aims and Hypothesis

This research will determine the extent to which alcohol and marijuana use contributes to the risk of metabolic syndrome among adults in the United States using data from the National Health and Nutritional Examination Survey.

The overall goals will be to explain the independent and interactive association of alcohol and marijuana use and metabolic syndrome. Also, the relationship between concurrent use of alcohol and marijuana, and metabolic syndrome will be examined. Gaining more knowledge about these association will add to the body of literature and assist in public health planning.

Aim 1: Determine the extent of the relationship between alcohol and marijuana use and metabolic syndrome.

Hypothesis 1*: Independent alcohol and marijuana use, compared to nonuse, will be associated with metabolic syndrome.*

Aim 2: Determine the association between concurrent use of alcohol and marijuana and metabolic syndrome.

Hypothesis 2*: concurrent use, compared to nonuse, will be associated with metabolic syndrome*

Aim 3: Determine the statistical interaction of alcohol and marijuana use on metabolic syndrome.

Hypothesis 3*: The effect of Marijuana use on metabolic syndrome is dependent on alcohol use.*

CHAPTER II – Literature Review

2.1. Alcohol and Metabolic Syndrome

According to the World Health Organization, alcohol is a psychoactive substance with dependent-producing qualities. Harmful use of alcohol is a significant public health concern in societies because it is implicated in more than 200 disease conditions. Its consumption is associated health problems such as alcohol dependence, noncommunicable diseases, such as liver cirrhosis, cardiovascular diseases, and some cancers.[10] Alcohol consumption is responsible for unintentional and intentional injuries, including those that result from violence, suicides, and road traffic accident.

Globally, about 13.5 grams of pure alcohol per day is consumed by persons aged 15 years or older, and harmful use of alcohol is responsible for 3.3 million deaths every year. Alcohol consumption is an important long-term risk factor for cardiovascular diseases such as hypertension, heart disease, and stroke. In the United States, it is responsible for 1 in 10 deaths among working-age adults aged 20-64 years. In 2010, the economic costs of excessive alcohol use were nearly $249 billion which translates to $2.05 per day.[10]

Several studies have focused on the impact of alcohol use on the risk of metabolic syndrome. Reports are unstable and controversial. Studies have found positive correlations,[11] others have found contrary[12] or no correlations between alcohol and metabolic syndrome.[13]

Djousse et al., (2004) in a cross-sectional study involving 4510 white participants of the National Heart, Lung, and Blood Institute Family Heart Study, examined the association between total and beverage-specific alcohol consumption and the prevalence odds of

Metabolic Syndrome. The authors observed reduced prevalence odds of metabolic syndrome across all beverage types: compared with never-drinkers, multivariate-adjusted odds ratios (95% confidence interval) of metabolic syndrome were 0.32 (0.14 to 0.73), 0.42 (0.23 to 0.77), 0.57 (0.30 to 1.09), and 0.56 (0.36 to 0.88) for subjects who consumed >7 drinks/week of wine only, beer only, spirits only, and more than one type of beverage, respectively. The writers concluded that irrespective of the type of beverage consumed, alcohol remains associated with a lower prevalence of Metabolic syndrome.[14]

Sun et al., (2014) examined the association between alcohol consumption and risk of metabolic syndrome in a meta-analysis of prospective studies. The authors analyzed data from six prospective studies involving 28,862 participants with 3305 cases of metabolic syndrome from different populations (2 studies in Asia, two studies in Europe and 2 in America). Compared with nondrinkers, very light drinker was associated with decreased risk of metabolic syndrome [pooled relative risk (RR): 0.86, 95% CL: 0.75-0.99] while heavy drinker was associated with increased risk of metabolic syndrome (pooled RR 1.84, 95% CI: 1.34-2.52). The article concluded that heavy alcohol consumption might be associated with an increased risk of metabolic syndrome. They cautioned, however, the fact that measurement of alcohol consumption is not standardized could complicate findings among studies.[15]

Yokoyama et al., (2007) examined the effect of alcohol consumption on the diagnosis of metabolic syndrome in a cross-sectional study of 2,130 Japanese men aged 20 to 65 years. The authors assessed excessive alcohol via questionnaire as people who consume more than 20g per day, and others were considered as average drinkers. The authors defined metabolic syndrome with the modified National Cholesterol Education Program: Adult Treatment Panel III

(NCEPATPIII) which require the presence of any three of the five components: central obesity, hypertension, hyperlipidemia, decreased high-density lipoprotein cholesterol, and raised fasting blood glucose for the diagnosis of metabolic syndrome. Prevalence of metabolic syndrome was significantly higher in excessive drinkers (22.2%) than average drinkers (13.9%, chi2 = 18.0, P<0.0001). Yokoyama et al. concluded heavy alcohol consumption might be a factor worsening metabolic syndrome.[11]

Santos, Ebrahim & Barros, (2006) conducted a cross-sectional study to determine the association of physical activity, sleeping hours, alcohol intake and smoking and metabolic syndromes. The authors examined self-reported social, demographic, personal and family medical histories and behavioral characteristics of 832 men and 1332 women aged 18—92 years. Alcohol consumption was assessed based on the type of alcoholic beverage and the amount in grams consumed, and metabolic syndrome was defined using the NCEP/ATP III criteria. After adjusting for age, education, physical activity, and smoking, there was no statistically significant relationship between ethanol intake and metabolic syndrome (aOR 1.56, 95% CI, 0.82, 2.96).[12]

Yokoyama, (2011) in another cross-sectional study involving 371 non-diabetic Japanese workers examined whether alcoholic beverages could be the remedies for insulin resistance that plays a pivotal role in the development of Metabolic syndrome. Yokoyama looked at the correlation between levels of ethanol consumption and insulin resistance. He assessed insulin resistance by using the homeostatic model assessment (HOMA). Yokoyama found that ethanol consumption was inversely correlated with insulin resistance levels. He noted, however, that such beneficial effects may not apply to subjects with obesity. Yokoyama also noted various

limitations due to the experimental design, including lack of information on the integrating amount of ethanol consumption, types of alcoholic beverage and precise evaluation of liver and pancreatic cirrhosis which can both play a role in insulin resistance.[16]

(Castelli et al., 1977; Macmahon, 1987 & Langer et al., 1992), revealed (as cited in Frujita & Takei, 2001) that regular, light to moderate consumption of alcohol could reduce the risk of coronary heart disease. The authors found that the beneficial effect of light to moderate alcohol consumption can be explained by several factors, including increases in the high-density lipoprotein cholesterol, while detrimental impacts of heavy alcohol use are due to an increase in plasma triacylglycerol and raised blood pressure.[4]

2.2. Alcohol and Components of Metabolic Syndrome

Several studies have shown that that alcohol consumption has independent effects on the components of metabolic syndrome. Yoon et al., (2004) examined the relationship between alcohol and the metabolic syndrome in a secondary analysis of 3597 men and 4365 women who had participated in the Korean National Health and Nutrition Examination Survey. The adjusted odds ratio for the metabolic syndrome in the group consuming < 15g of alcohol /day was 0.71 (95% CI: 0.53, 0.95) in men and 0.80 (95% CI: 0.65, 0.98) in women. Also, heavy alcohol consumption (≥ 30g/d) was associated with significantly higher odds ratios for high blood pressure and high triacylglycerol in men, and high fasting blood glucose and high triacylglycerol on women.[17]

Kim et al., (2017) evaluated the relationship between alcohol consumption and Metabolic syndrome components in a community-based cohort of 10,037 subjects. The authors

found that among men, compared to non-drinker, consumption of >30 g/day showed significant association with high blood pressure (OR 1.63 95% CI: 1.36-1.94), high fasting glucose (OR 1.88 95% CI: 1.40-2.51), hypertriglyceridemia (OR 1.77 95% CI: 1.44-2.04) and inverse association with low HDL cholesterol (OR 0.30 95% CI: 0.25-0.36). The study also found a similar association between light and moderate drinkers. Among women, the authors found that heavy drinkers (>30 g/day) are likely to have high fasting glucose (OR 3.50 95% CI: 1.41-8.71) compared to non-drinkers. The authors concluded that daily alcohol consumption of >5g/day might contribute to abnormalities of Metabolic syndrome including high glucose and blood pressure, hypertriglyceridemia, and low HDL cholesterol.[18]

Most prospective cohorts reviewed revealed that risk of obesity/weight gain, an essential component of IDF definition metabolic syndrome depends on the amount and type of alcoholic beverage consumed. Schütze et al., (2009) in a prospective European study, examined associations between beer consumption and waist circumference (WC). In a secondary analysis of 7876 men and 12749 women within the European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam study. Men who consumed 1000ml of beer/day had 17% higher WC compared with light drinkers (≥ 250 to <500ml/day). In women, there was a significant inverse relationship between beer-abstaining women and WC gain (odds ratio: 0.88 95% CI: 0.81, 0.96) compared to very-light drinking women. However, after adjusting for concurrent body weight and hip circumference, a non-significant association was observed.[19]

MacInnis et al., (2013) evaluated the predictors of increased adiposity for different measures of adiposity in a prospective cohort study of 5879 Australian-born participants, aged 40 to 69 years with data collected at baseline (1990—1994) and wave 2 (2003—2007). Subjects

who consumed low to moderate amounts of alcohol were less likely to have elevated waist circumference at wave 2. The authors concluded that limiting alcohol intake could be one of the promising ways of preventing obesity in adults.[20]

In another prospective study by Rissanen et al., (1991), 12,669 adults were examined twice with a median interval of 5.7 years. The authors found that heavy drinking was associated with substantial weight gain in women.[21]

2.3. Marijuana

Marijuana consists of over 421 components and 60 pharmacologically active cannabinoids. The two most well-known and understood cannabinoids are delta9-tetrahydrocannabinol (THC) and cannabidiol (CBD). Other components are not fully understood, and their mental and physical effects are unknown.[22]

Marijuana also known as cannabis act via two receptors; CB1 and CB2. CB1 is mainly found in the brain and the spinal cord while CB2 receptors are predominately expressed in the peripheral tissues of cells in the immune system, hematopoietic system, and reticuloendothelial system. Moreover, acts majorly on the brain and spinal cord.[22]

Marijuana has many documented toxic effects including acute effects like; impairment of cognitive and psychomotor function.

Chronic effect of cannabis use includes cannabis dependence syndrome, exacerbation of symptoms in schizophrenic patients, epithelial injury of the respiratory system, and increased prevalence of chronic bronchitis.[23]

2.4 Marijuana Prevalence

According to the Center for Disease Control (CDC), marijuana is the most commonly used illegal drug in the united states with about 22.2 million users every month,[3] and it has a very high index for addiction. Research shows that 1 in every ten marijuana users will become addicted.[24] Worldwide, it is the most used illicit drug, about 2.5% of the world population consume cannabis which is higher than 0.2% consuming cocaine and 0.2% consuming opiates.[22]

With the decriminalization and legalization of marijuana, the significant public health concern is that its legalization will increase its use. Currently, 23 states and territories in the USA have legalized medical marijuana use, and recreational use is now legal in four states.[25]

2.5. Marijuana and Metabolic Syndrome

Evidence from studies suggests that marijuana use influences the cardiovascular physiology. It increases heart, systolic and diastolic blood pressures; these actions increase the oxygen demand of the myocardium.[7]

The risk of cardiovascular disease increases by about five times for users and more for users with pre-existing conditions.[26] Metabolic syndrome is a well-known major risk factor for cardiovascular diseases; therefore, it is relevant to review marijuana's effect on the syndrome.

Franz & Frishman 2016, evaluated recreational marijuana and cardiovascular disease, the authors found that smoking marijuana increases the risk of myocardial infarction by a factor of 4.8 for the 60 minutes after marijuana use. Franz and Frishman recommended against the recreational marijuana use, especially in individuals with a history of coronary artery diseases.[7]

Vidot et al., (2015) used data from a representative study of US adults aged 20- to 59-years, the National Health and Nutrition Examination Survey (NHANES), to explore the

relationship between marijuana use and metabolic syndrome. The investigators found that current marijuana users had lower odds of metabolic syndrome than never users (adjusted odds ratio [AOR] 0.69; 95%confidence intervals [CI], 0.47-1.00; P =. 05). Besides, among emerging adults (20-30 years old), current marijuana users were 54% less likely than never users to present with metabolic syndrome. Compared with never users, past (AOR 0.61; 95% CI, 0.40-0.91) and current (AOR 0.49; 95% CI, 0.25-0.97) middle -age marijuana users were less likely to develop metabolic syndrome.[27]

Thompson and Hay, (2015) in a cross-sectional study examined the relationship of metabolic risk factors and marijuana use in U.S. adults using the data from the continuous National Health and Nutrition Examination Survey (NHANES). Using the data on from 6281 participants and computing the ordinary least squares (OLS) models, revealed that fasting insulin, insulin resistance, body mass index, and waist circumference were all significantly lower in current marijuana users compared to lifetime non-users. To test the reliability of the model, the researchers substituted marijuana use with alcohol use as the risk factor of interest; the result was like the estimates of the effect of marijuana use. The authors concluded that while current users of marijuana may less likely develop metabolic syndrome, OLS regression might not be a reliable model to examine the association.[8]

Muniyappa et al., (2013) also examined the metabolic effect of chronic cannabis smoking. In the cross-sectional case-control study, 18 men and 12 women aged 27 ± 8 years were matched for sex, age, body mass index and ethnicity with 30 controls. The authors found that chronic cannabis smoking was associated with visceral adiposity (18 ± 9 vs. 12 ± 5%;

p=0.004). lower HDL cholesterol (49 ± 14 vs. 55 ± 13 mg/dL; p= 0.02), and adipose tissue insulin resistance,[28] all components of metabolic syndrome.

Le Strat and Le Foll, (2011) analyzed data from 2 cross-sectional epidemiologic studies of US adults aged 18 years or older, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; 2001–2002) and the National Comorbidity Survey–Replication (NCS-R; 2001–2003). The specific aim was to estimate the prevalence of obesity as a function of cannabis use. The authors found that adjusted prevalence of obesity in the NESARC and the NCS-R were 22.0% and 25.3%, respectively among subject reporting no use of cannabis in the past 12 months and 14.3% and 17.2%, respectively, among participants reporting the use of cannabis at least three days per week. Additionally, after adjusting for sex and age, the use of cannabis was associated with body mass index differences in both samples. The authors concluded that the prevalence of obesity is lower in cannabis users than in nonusers.[29]

In a recent study, Yankey et al., (2017) evaluated the relationship between years of self-reported marijuana use and metabolic syndrome using the National Health and Nutrition Examination Survey (NHANES) 2011-2012. Surprisingly, irrespective of the criteria used, the adjusted odds ratio (aOR) for having metabolic syndrome with each increase in year of marijuana use. The aOR was 1.05 (95% CI: 1.02, 1.08), 1.08 (95% CI: 1.04, 1.13) and 1.05 (95% CI: 1.04, 1.13) for National Cholesterol Education Program Adult Treatment Panel III (ATP III), International Diabetes Federation (IDF), and World Health Organization (WHO) respectively. Furthermore, the authors found a significant association between each year of marijuana use and components of metabolic syndrome (hypertension and abdominal obesity). The adjusted OR of Hypertension was 1.05 (95% CI: 1.01, 1.09) for WHO criteria and 1.08 (95% CI: 1.03, 1.12)

using EGIR. Irrespective of the criteria, each year of marijuana use was associated with increased odds for abdominal obesity: aOR 1.06 (95% CI: 1.00, 1.11) (ATP III), 1.09 (95% CI: 1.05, 1.14) (EGIR), and 1.07 (95% CI: 1.01, 1.13) (IDF). The authors concluded that recreational marijuana use might be detrimental to cardiovascular health.[30]

2.6. Alcohol and Marijuana co-use and Metabolic Syndrome.

The decriminalization and legalization of marijuana coupled with the consumption of alcohol in significant amounts raise a public health concern. Pacula and Sevigny, (2014) argued that marijuana liberalization policies could lead to increases in both alcohol and marijuana use, hence the need to fully understand the association between these two substances, especially about their public health consequences.[31]

Subbaraman & Kerr, (2015) examined the differences in demographics, alcohol-related social consequences, harms to self, and drunk driving across simultaneous, concurrent and alcohol-only groups. The authors conducted a secondary analysis of data from the 2005 and 2010 National Alcohol Survey involving 4,522 females, and 4,104 males. The authors found that individuals who used both cannabis and alcohol tend to use them at the same time (simultaneous use). Also, compared with alcohol only use, the odds of drunk driving, social consequences, and harms to self is two times among simultaneous users.[5]

Alcohol consumption and marijuana use have independently been associated with metabolic syndrome. However, little or no study has examined the combined effects of alcohol consumption and marijuana use on metabolic syndrome. Findings from the literature reviewed suggest that interaction of these drugs may result in detrimental effect. This thesis will also

examine the interaction of alcohol consumption and marijuana use on metabolic syndrome. Understanding the interaction between alcohol and marijuana and the risk of metabolic syndrome will add to the body of knowledge, assist in policy initiatives and the implementation of effective preventive strategies against cardiovascular diseases.

CHAPTER III – METHODOLOGY

3.1. Study Design

This research will analyze data from the National Health and Nutrition Examination Survey (NHANES). NHANES is a scheme of studies that assess the health and nutritional status of adults and children in the United States. It is under the oversight of National Center for Health Statistics (NCHS), a division in the Centers for Disease Control and Prevention with the responsibility of producing vital and health statistics for the country.

The program started over five decades ago, and it is an ongoing revolving survey that addresses the health and nutritional topics of different populations. The survey examines about 5,000 nationally representative sample annually, located in various counties across the nation, fifteen of which are visited.

The survey has two components; Using Computer-Assisted Personal Interview Technology (CAPI), for conducting an initial in-person interview in the participant's home, and it includes; demographic, socioeconomic, dietary health-related questions. The examination component which consists of medical, dental, physiological measurements, and laboratory tests conducted by highly trained medical personnel in specifically designed mobile examination centers (MEC). This survey collects information on prevalence of chronic conditions in the population. Also, it provides an estimate of previously undiagnosed conditions as well as aspects of a person's lifestyle, heredity, constitution, or environment that may increase the chances of developing a specific disease

Data of this survey are used in epidemiological studies and health sciences research, which help build effective public health initiative and policy. Also, information from the survey helps the public health professionals determine disease prevalence and predisposing factors, assess nutritional status and its association to health promotion and prevention.

Eligibility criteria: adults ≥ 20 years who were involved in the 2012-2013 NHANES were included in the study.

Variables of Interest

Dependent Variable

Metabolic Syndrome

Metabolic Syndrome was defined using the International Diabetes Federation (IDF) criteria. These criteria were used because central obesity which is the driver for most cardiovascular diseases was used as the primary criterion. It is also a universally accessible, diagnostic tool that addresses both clinical and research needs by providing a comprehensive list of criteria including ethnic specific cut-off points that should be included in research into the metabolic syndrome.

IDF defined Metabolic Syndrome as the presence of:

Central Obesity: defined as waist circumference with ethnicity-specific values; ≥ 102 cm (white males) or ≥ 88 cm (white females); ≥ 94 cm (black males) or ≥ 80 cm (black females); ≥ 94cm (Mexican American/Multiracial males) or ≥ 80 cm (Mexican American/Multiracial females). The IDF recommends ethnic group-specific cut-points should be used for people of the same ethnic group wherever they are found. Thus, the criteria recommended for central

Americans was also be used in Mexican Americans, as would those for central Americans males and females regardless of place and country of residence.

Plus any two of the following: raised triglycerides ≥ 150mg/dL or on treatment for this lipid abnormality; reduced HDL cholesterol <40 mg/dL in males and < 50mg/dL in females or on treatment for this lipid abnormality; raised blood pressure systolic blood pressure ≥ 130 or diastolic blood pressure ≥ 85 mm Hg or on treatment for previously diagnosed hypertension; raised fasting plasma glucose (FPG) ≥ 100mg/dL, or previously diagnosed type 2 diabetes.

Information about laboratory and clinical procedures are well-documented in the NHANES manual.[32]

Independent Variables

Main independent variables were marijuana and alcohol use.

Marijuana Use

Marijuana use was categorized into current marijuana users (those who have used marijuana before and at least ≥ one day in the last 30days), and never marijuana users (never used marijuana). The definition was based on the following questions: 1.) Ever used marijuana or hashish? 2.) During the past 30 days, on how many days did you use marijuana or hashish?

Alcohol Use

Alcohol use was categorized into nondrinkers (have not had any drink in the past 12 months and not up to 12 drinks in their entire lifetime), current drinkers (had at least 12 drinks in the past year and had a drink at least ≥ one day in the last 30 days). According to the National Institute on Alcohol Abuse and Alcoholism, current drinkers were further divided into low/moderate drinkers (men: up to 2 drinks per day, women: up to a drink per day), and heavy

drinker (men: 4 or more drinks on any day, women: 3 or more drinks on any day).[33] Alcohol use definition was based on the following questions; 1.) In your entire life, have you had at least 12 drinks of any alcoholic beverage? 2.) In any one year, have you had at least 12 drinks of any type of alcoholic beverage. 3.) In the past 12 months, on those days that you drank alcoholic beverages, on the average, how many drinks did you have? 4.) How many days per week, per month, or per year did you drink alcohol?

Concurrent Use

Based on the current drinking and marijuana status, a new indicator variable addressing concurrent use was created. Concurrent users were categorized as Yes: (if classified as both current drinker and current marijuana user) and No (classified as either a current drinker or current marijuana user).

Other Independent Variables

Age

Reported as the age in years at the time of participation. Participants were evenly distributed across three age categories young adults (20-35) years, middle-aged adults (36-55) years and older aged adults (> 55) years

Race

Categorized into White, African American, Hispanics, and Other Race/Multi-racial

Gender

Gender of the participant at the time of screening. Grouped into male and female based on self-reported data.

Educational level

Categorized into ≤ High School and > High school.

Family to income ratio (PIR)

PIR denotes the ratio of the family's income to the poverty threshold. PIR was used in this study as a measure of socioeconomic status. Based on the standard recommended by United States Poverty Guideline 2018, participants' PIR was classified into three categories; < 1.00, 1.00 - 4.00, and > 4.00.

Marital status

For this study, participant's marital status is categorized as Married and Others.

Physical Activity

Physical activity was categorized into two groups: physically active and physically inactive. Participants were allocated to this group based on their response to the following questions from the NHANES questionnaire: "In a typical week do you do any vigorous-intensity sports, fitness, or recreational activities that cause large increases in breathing or heart rate like running or basketball for at least 10 minutes continuously?" or " In a typical week do you do any moderate-intensity sports, fitness, or recreational activities that cause a small increase in breathing or heart rate such as brisk walking, bicycling, swimming, or volleyball for at least 10 minutes continuously?" participants that responded 'yes' to either of the aforementioned questions were classified as physically active while those that responded 'no' were allocated to the physically inactive group.

Cigarette Smoking

Current cigarettes smokers: Participants who reported they had smoked at least 100 cigarettes in their lifetime, and still smoke on some days or every day. Past smokers: participants who have smoked at least 100 cigarettes in their lifetime but do not currently smoke. Never smoker: those who have never smoked cigarettes.

3.2. **Statistical Analysis**

All analyses were performed using SAS 9.4 (Statistical Analysis System, Cary, NC, USA). In 2013-2014, NHANES included 14,332 persons selected from 30 different survey locations to participate in the study. Of those selected, 10,175 and 9,813 completed the interview and examination respectively. For this thesis, the sample size was 2,142 (20 years and older).

Descriptive statistics were conducted for all participant characteristics including age, gender, race, marital status, education, and family to income ratio (PIR). Bivariate analyses were conducted using Chi-Square Test for categorical variables and the Wilcoxon Rank sum test for continuous variables.

Multivariable logistic regression models were constructed to explore the effects of the primary independent variables on metabolic syndrome. The logistic regression results are reported as odd ratios (OR) and 95% confidence interval (CI). A Stepwise selection method was used to identify the significant predictors of metabolic syndrome. A significance level of 0.3 is required to allow a variable into the model (SLENTRY= 0.3), while a significance level of 0.35 is required for a variable to stay in the model (SLSTAY= 0.35). The final model included variables fitted by stepwise selection and a priori, potential confounders identified by the bivariate analysis. Overall, three models were fitted – alcohol consumption, marijuana use, & concurrent

use. The statistical interaction between alcohol consumption and marijuana use was also assessed using their product term, with the level of significance determined using the likelihood ratio test. A two-sided P value < 0.05 was considered statistically significant for all analyses.

CHAPTER IV – RESULTS

4.1. Descriptive Statistics

Overall, 2,239 participants aged 20 years and older were included in this analysis. The demographic and other characteristics of participants who self-reported for alcohol and marijuana use were similar. Participants with missing data on the variable of interest were excluded. Most respondents were between 35 and 55 years, and nearly half of the participants who self-reported for alcohol and marijuana were whites (34%-41.6%). Majority attained above high school education (59% – 62.6%), are physically inactive (62% – 63.2%) and met the IDF definition for central obesity (67%).

Alcohol Use Characteristics

Of the participants, 930 (77.2%) were current drinkers, and 275 (22%) were non-drinkers. 55.5% are males, and 45.5 % are females. Current drinkers are mostly young adults (37.9%) and middle-aged adults (41.6%). White Americans consume alcohol at the highest rate among major ethnic groups (45.4%), followed by blacks (21.6%), Hispanics (20.4%), and other races (12.6%). Almost have of current drinkers had above high school education (65.0%), are physically inactive (60.9%) and are current smokers (26.8%). (Table 1.1).

The Proportion of Central obesity among current drinkers was 57.8% compared to 70.8% among non-drinkers ($P < 0.01$). Prevalence of raised fasting blood glucose, raised systolic blood pressure, and low HDL cholesterol was similar in the participants who were current and non-drinkers.

Marijuana Use Characteristics

There were 223(23.8%) current users and 714(76.2%) never users of marijuana. Majority of current users are young (64.6%). Marijuana use was highest among whites (46.6%), followed by blacks (29.6%), Hispanics (14.8%) and other races (9%). Males are nearly twice as likely (62.8%) to use marijuana as females (37.2%). Current marijuana use is also more common among participants who are not legally married (78%), had above high school education (52%), physically inactive (51.1%) and current smokers (56.5%).

Participants who reported current use of marijuana have significantly lower body waist circumference (median 89.6 vs 95.5 cm, P = < 0.01), fasting plasma glucose (median 95.0 vs 97 mg/dl, P = < 0.01), and diastolic blood pressure (median 68 vs 72 mmHg, P = <0.01) compared to those who never smoked marijuana.

Metabolic Syndrome

Metabolic syndrome prevalence among participants using International Diabetes Federation (IDF) criteria was 29.2%. A Majority were 36 years and older. Prevalence of metabolic syndrome was 24.1%, 17.7%, and 13.6%, among current drinkers, current marijuana users, and concurrent users respectively.

4.2. Result of Bivariate Analysis

Alcohol and Participant's characteristics

Results revealed a statistically significant difference between alcohol and each of the participant's characteristics (age, gender, race, education, family to income ratio, physical activity, smoking- P < 0.01 for all). There was a statistically significant difference between

alcohol use and body waist circumference (P < 0.01), HDL cholesterol (P < 0.01). There was no significant difference observed between alcohol use and fasting plasma glucose, triglyceride level, systolic and diastolic blood pressure (Table 1.1).

Marijuana and Participant's characteristics (Table 1.2)

Furthermore, a statistically significant difference was observed between marijuana use and each of the following participant's characteristics (age, gender, race, marital status, family to income ratio, physical activity, education and cigarette smoking- P < 0.01 for all). A similar result was found between marijuana use and some components of metabolic (body waist circumference [P < 0.01] and fasting plasma glucose [P < 0.01]).

Metabolic Syndrome and Participant's characteristics (Table 1.3)

The Chi-square test of association between metabolic syndrome and each of the participant's characteristics (age group, race, education, marital status, family to income ratio, and cigarette smoking- P < 0.01 for all) found a statistically significant difference between the variables. There was a statistically significant difference between metabolic syndrome and each of the two primary independent variables (alcohol and marijuana use, P = 0.02).

4.3. Result of Multivariate Analysis

In the unadjusted analysis, current drinkers were less likely to have metabolic syndrome compared to non-drinkers (odds ratio [OR], 0.69 95% confidence interval [CI], 0.51-0.94). The analysis also revealed similar associations for both current marijuana users and concurrent users, with OR, 0.59 95% CI, 0.40-0.86 and OR, 0.44 95% CI, 0.26-0.73 respectively. The odds of metabolic syndrome were lower participants that consume low/moderate alcohol compared to non-drinkers OR, 0.70 95% CI, 0.49, 0.99 (Table 3.1).

Table 2.1, 2.2, and 2.3 give a summary of the stepwise logistic regression model selection. After adjusting for age, race, educational level, marital status, poverty, and cigarette smoking status; current drinkers showed a significant inverse association with metabolic syndrome (adjusted odds ratio [aOR], 0.69 95% confidence interval [CI], 0.49-0.99). In the same multivariable model, compared with participants aged 20-35 years, adults between 36 and 55 years (aOR, 2.57 95% CI, 1.80-3.68) and above 55 years (aOR, 3.36 95% CI, 2.26-4.99) had higher odds of metabolic syndrome. Participants who are past smokers had more odds developing metabolic syndrome compared to non-smokers. The odds of metabolic syndrome among current marijuana users was lower compared to never users, although this association was not significant (aOR, 0.62 95% CI,0.38, 1.01).

Similarly, the odds of Metabolic syndrome among concurrent users was 0.53 times the odds of metabolic syndrome among non-concurrent users (95% CI, 0.28-0.99). In both marijuana and concurrent model, being 36 years and older was significantly associated with increased odds of metabolic syndrome (Table 3.2). Test for statistical interaction between alcohol consumption and marijuana use revealed no statistically significant result, and thus the product term was not included in the model.

CHAPTER V – Discussion

5.1. Discussion

The purpose of this thesis was to evaluate alcohol and marijuana use interaction on metabolic syndrome among United States adults. Marijuana remains a commonly used illicit drug among those who drink, coupled with the swift evolution of marijuana policies over the years, there a need to understand the interaction of these two drugs and its adverse metabolic outcomes.

This study was conducted by using NHANES data, a survey that examines the nationally representative sample of about 5,000 persons per year. The survey collects data on the prevalence of chronic conditions in the population as well as information on aspects of a person's lifestyle, heredity, constitution, or environment that may increase the chances of developing a specific disease. The survey also employed the use of Computer-Assisted Personal Interview Technology (CAPI), this allows for clarification and ascertainment of responses.

Overall, results from this study suggest that current drinkers, current marijuana users, and concurrent users were associated with decreased odds of metabolic syndrome. Adjusting for age group, race, educational level, marital status, cigarette smoking, and family to income ratio; the negative association remained significant with a notable exception for current marijuana users. The analysis also found that among current drinkers, those who consumed low to moderate proportion of alcohol have lower odds of metabolic syndrome. Participants who were 36 years and above were consistently associated with increased odds of metabolic syndrome in all three models.

Most researchers have focused on the independent relationship of alcohol and marijuana use on metabolic syndrome. This thesis is probably the first study till date to examine the association between concurrent alcohol/marijuana use and its effect on metabolic syndrome. Although, this analysis observed an inverse association between concurrent use and metabolic syndrome (aOR, 0.53 95%, 0.28-0.99), still, cautious interpretation of this result is needed. This observed association could be because of how concurrent use was assessed. It is important to note that, questions relating to the concurrent use of alcohol and marijuana were not directly asked in the NHANES data, and therefore the assessment of concurrent use could be biased. It is imperative to conduct further longitudinal studies to confirm if the observed association is indeed true.

The observed inverse association between alcohol use and metabolic syndrome is similar to findings from previous studies. Djousse et al., (2004) cross-sectional survey of participants of the National Heart, Lung, and Blood Institute Family Heart Study reported reduced prevalence odds of metabolic syndrome among alcohol users across all beverage types: OR, 95% -- 0.32 (0.14 to 0.73), 0.42 (0.23 to 0.77), 0.57 (0.30 to 1.09), and 0.56 (0.36 to 0.88) for subjects who consumed more than 7 drinks/week of wine only, beer only, spirits only, and more than one type of beverage, respectively.[14] The result of this study is not comparable to this present study because the authors computed beverage-specific alcohol concentrations, and the reported association was not consistent across all beverage groups.

This thesis also found that low/moderate intake of alcohol is associated with lower odds of metabolic syndrome. Earlier studies have also reported similar association. A prior meta-analysis of six prospective studies in 2014 including 28,862 participants found that very light

drinkers have a decreased risk of metabolic syndrome (Pooled RR: 0.86, 95% CL: 0.75-0.99).[15] The research was more superior because the authors conducted a meta-analysis of prospective studies with no evidence of heterogenicity or publication bias between the very light and heavy alcohol groups. However, non-standardized methods for assessing alcohol consumption noted in the study could complicate interpretation of findings among studies. On the other hand, people that consume alcohol in low to moderate proportion usually opt for wine instead of beer and spirit. It is plausible to say that the observed inverse association may be due to other substances found in wine rather than the ethanol itself.

Also, studies have also found conflicting results on whether alcohol use has a protective or detrimental effect on metabolic syndrome. Alcohol has a variable effect on components of metabolic syndrome. Freiberg et al., (2003) in a cross-sectional analysis on data from 8,125 participants from the Third National Health and Nutrition Examination Survey reported that alcohol use was significantly and inversely associated with the prevalence of the following three components of the metabolic syndrome: low serum HDL cholesterol, elevated serum triglycerides, high waist circumference, as well as hyperinsulinemia ($P < 0.05$ for all). Thus, the inverse relationship observed may differ based on the metabolic profile of the group being studied.

Notably, in all the models constructed, being 36 years and older have higher odds of metabolic syndrome, and this was consistent with previous studies that reported that prevalence of metabolic syndrome increases with age. [34] A previous cross-sectional survey in 2012 reported age might influence the relationship between alcohol and metabolic syndrome.[35] In all the models constructed for this study, compared to young adults aged 20-35 years,

participants between 36-55 years are over two times likely to have metabolic syndrome and those >55 years are over three times more likely to develop the syndrome. It will be imperative to understand age-specific relationship between alcohol, marijuana, and metabolic syndrome.

Another finding from this research indicates that past smokers have higher odds of metabolic syndrome. A similar association was observed in previous studies.[36] A 2015 study reported that former smokers had a higher risk of metabolic syndrome compared to light smokers (pooled RR 1.19, 95% CI: 1.00–1.42).[37] These findings could be because smoking is strongly associated with obesity, a significant determinant in the IDF definition used for this study, and higher odds of metabolic syndrome further support the hypothesis that smoking has a peripheral metabolic effect in the body. Smokers are likely to have reduced calorific intake, which translates to less absorption and storage of fats in adipose tissues. The cessation of smoking reverses this process.[37]

5.2. Study Limitations and next steps

Despite apparent strength of using a nationally representative survey for this analysis, this study is subject to limitations. Firstly, the NHANES is cross-sectional; no casual inferences can be made from these data. This design cannot establish temporality because information about whether the alcohol or marijuana use preceded the development of metabolic syndrome is not available. The possibility of reverse causality bias cannot be ruled out. More detailed longitudinal studies are required to confirm these findings. Secondly, alcohol and marijuana use were also accessed via self-report data which are subject to reporting bias. There's no way to ensure that respondents gave accurate answers to questions or just gave a socially desirable

response. Biochemical verification may be necessary for objective assessment of these responses.

5.3. Conclusion

The result of this study suggests that there an inverse relationship between alcohol, concurrent alcohol & marijuana use, and metabolic syndrome. However, interpretation should be made with caution. With the evolving climate of decriminalization of marijuana and limited research on its potential health effects, policymakers, especially at the state level should understand this lack of knowledge is a notable barrier not only to scientific understanding but also to the improvement of public policy and public health of the populace.

The public should be made aware of the role of increasing age and smoking as important predictors of metabolic syndrome and the need to institute lifestyle modifications in high-risk groups.

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Table 1.1 Participants Characteristics stratified by Alcohol Use

	Alcohol Use		Total	P-value
	Current Drinker	Non-Drinker		-
Demographics	**N (%) = 930 (77.2)**	**N (%) = 275 (22.8)**	**1205**	
Age				
Median (IQR)	41.0 (29.0-53.0)	47.0 (32.0-58.0)	45.0 (33.0-57.0)	**<0.01** [w]
20-35	352 (37.9)	81 (29.5)	433 (35.9)	**<0.01**[c]
36-55	387 (41.6)	102 (37.1)	489 (40.6)	
>55	191 (20.5)	92 (33.4)	283 (23.5)	
Gender				**<0.01**[c]
Female	414 (44.5)	197 (71.6)	611 (50.7)	
Male	516 (55.5)	78 (28.4)	594 (49.3)	
Race				**<0.01**[c]
Hispanic	190 (20.4)	70 (25.5)	260 (21.6)	
White	422 (45.4)	76 (27.6)	498 (41.3)	
African- American	201 (21.6)	54 (19.6)	255 (21.2)	
Other Race/Multi-racial	117 (12.6)	75 (27.3)	192 (15.9)	
Education				**<0.01**[c]
≤ High School	325 (35.0)	125 (45.6)	450 (37.4)	
> High School	604 (65.0)	149 (54.4)	753 (62.6)	
Marital Status				**0.03**[c]
Married	468 (50.3)	159 (57.8)	627 (52.0)	
Others	462 (49.7)	116 (42.2)	578 (48.0)	
Poverty to Income Ratio				
Median (IQR)	2.7 (1.2-4.9)	1.64 (0.9-3.3)	2.1 (1.0-4.2)	**<0.01** [w]
<1.00	219 (23.6)	100 (36.4)	319 (26.5)	**<0.01** [C]
≥1.00-4.00	399 (42.9)	135 (49.1)	534 (44.3)	
>4.00	312 (33.5)	40 (14.6)	352 (29.2)	
Physical Activity				**<0.01**[c]
Active	364 (39.1)	79 (28.7)	443 (36.8)	
Inactive	566 (60.9)	196 (71.3)	762 (63.2)	
Cigarette Use				**<0.01**[c]
Current Smoker	249 (26.8)	19 (6.9)	268 (22.2)	
Past Smoker	199 (21.4)	16 (5.8)	215 (17.8)	
Non-smoker	482 (51.8)	240 (87.3)	722 (59.9)	
Clinical Information				
Body waist circumference, cm				
Median (IQR)	97.0 (91.0-105.0)	95.5 (84.4-108.0)	97.0 (86.0-108.0)	0.21
Central Obesity	530 (57.8)	187 (70.8)	717 (60.7)	**<0.01**[c]
Normal	387 (42.2)	77 (29.2)	464 (39.3)	
Fasting plasma glucose, mg/dl				
Median (IQR)	95.2 (84.8-106.6)	99.0 (91.0-107.0)	98.0 (92.0-108.0)	0.20[w]
< 100	523 (58.0)	148 (55.4)	671 (57.4)	0.46[c]
≥ 100	379 (42.0)	119 (44.6)	498 (42.6)	
Blood Pressure, mmHg,				
Systolic blood pressure				
Median (IQR)	118.0 (108-128)	118.0 (108-130)	118.0 (108-128)	0.53[w]
< 130	666 (76.6)	186 (73.5)	852 (75.9)	0.31[c]
≥ 130	203 (23.4)	67 (26.5)	270 (24.1)	
Diastolic blood pressure				
Median (IQR)	70.0 (64.0-76.0)	70.0 (64-78.0)	70.0 (64.0-78.0)	
< 85	785 (90.3)	232 (91.7)	1017 (90.6)	0.63[w]
≥ 85	84 (9.7)	21 (8.3)	105 (9.4)	0.51[c]
HDL Cholesterol, mg/dl				
Median (IQR)	53.0 (43.0-63.0)	52.0 (43.0-64.0)	51.0 (42.0-62.0)	0.87[w]
Low	219 (24.4)	91 (34.3)	310 (26.7)	<0.01[c]
Normal	679 (75.6)	174 (65.7)	853 (73.3)	
Triglyceride, mg/dl				
Median (IQR)	89.0 (62.0-136.0)	94.0 (67.0-138.0)	94.0 (64.0-143.0)	0.23[w]
High	203 (22.6)	59 (22.3)	262 (22.5)	0.91[c]
Normal	695 (77.4)	206 (77.7)	901 (77.5)	

Abbreviations: IQR, interquartile range; ARV, antiretroviral.

[c] Chi-square statistical test was used to test for association

[w] Wilcoxon rank sum test was used to test for median difference

*P-value highlighted in bold indicate the finding is statistically significant at α=0.05 (p< .05)

Table 1.2 Participants Characteristics stratified by Marijuana Use

	Marijuana Use		Total	P-value
	Current User	Never User		-
Demographics	**N (%) = 223 (23.8)**	**N (%) = 714 (76.2)**	**937**	
Age				
Median (IQR)	30.0 (24.0-43.0)	41.5 (31.0-50.0)	45.0 (33.0-57.0)	**<0.01**[w]
20-35	144 (64.6)	237 (33.2)	381 (40.7)	**<0.01**[c]
36-55	72 (32.3)	406 (56.9)	478 (51.0)	
>55	7 (3.1)	71 (9.9)	78 (8.3)	
Gender				**<0.01**[c]
Female	83 (37.2)	427 (59.8)	868 (48.6)	
Male	140 (62.8)	287 (40.2)	919 (51.4)	
Race				**<0.01**[c]
Hispanic	33 (14.8)	232 (32.5)	265 (28.3)	
White	104 (46.6)	218 (30.5)	322 (34.4)	
African- American	66 (29.6)	110 (15.4)	176 (18.8)	
Other Race/Multi-racial	20 (9.0)	154 (21.6)	174 (18.6)	
Education				**0.02**[c]
≤ High School	107 (48.0)	277 (38.8)	384 (41.0)	
> High School	116 (52.0)	437 (61.2)	553 (59.0)	
Marital Status				**<0.01**[c]
Married	49 (22.0)	440 (61.6)	489 (52.2)	
Others	174 (78.0)	274 (38.4)	448 (47.8)	
Poverty to Income Ratio				
Median (IQR)	1.3 (0.69-2.8)	2.3 (1.0-4.3)	2.1 (1.1-4.2)	**<0.01** [w]
<1.00	93 (41.7)	211 (29.6)	304 (32.4)	**<0.01** [C]
≥1.00-4.00	97 (43.5)	322 (45.0)	419 (44.8)	
>4.00	33 (14.8)	181 (25.4)	214 (22.8)	
Physical Activity				**<0.01**[c]
Active	109 (48.9)	240 (33.6)	349 (37.2)	
Inactive	114 (51.1)	474 (66.4)	588 (62.8)	
Cigarette Use				**<0.01**[c]
Current Smoker	126 (56.5)	72 (10.1)	198 (21.2)	
Past Smoker	25 (11.2)	69 (9.7)	94 (10.0)	
Non-smoker	72 (32.3)	573 (80.3)	645 (68.8)	
Clinical Information				
Body waist circumference, cm				
Median (IQR)	89.6 (80.7-101.3)	95.5 (84.4-108.0)	95.6 (85.2-107.1)	**<0.01**[w]
Central Obesity	98 (44.6)	470 (67.1)	568 (61.7)	
Normal	122 (55.4)	230 (32.9)	352 (38.3)	
Fasting plasma glucose, mg/dl				
Median (IQR)	95.0 (89.0-101.0)	97.0 (92.0-105)	98.0 (92.0-108.0)	**<0.01**[w]
< 100	151 (70.6)	408 (58.5)	559 (61.4)	**<0.01**[c]
≥ 100	63 (29.4)	289 (41.5)	352 (38.6)	
Blood Pressure, mmHg,				
Systolic blood pressure				
Median (IQR)	116.0 (108.0-127.0)	116.0 (108.0-126)	118.0 (108-128)	0.78[w]
< 130	173 (81.6)	540 (81.2)	713 (81.3)	0.89[c]
≥ 130	39 (18.4)	125 (18.8)	164 (18.7)	
Diastolic blood pressure				
Median (IQR)	68.0 (60.0-74.0)	72.0 (64-78.0)	70.0 (64.0-78.0)	
< 85	194 (91.5)	599 (90.1)	793 (90.4)	**<0.01**[w]
≥ 85	18 (8.5)	66 (9.9)	84 (9.6)	0.54[c]
HDL Cholesterol, mg/dl				
Median (IQR)	51.0 (42.0-60.0)	51.0 (43.0-62.0)	51.0 (42.0-62.0)	0.57[w]
Low	54 (25.4)	212 (30.6)	266 (29.3)	0.15[c]
Normal	159 (74.6)	482 (69.4)	641 (70.7)	
Triglyceride, mg/dl				
Median (IQR)	86.0 (59.0-135.0)	94.0 (64.0-141.0)	94.0 (64.0-143.0)	0.16[w]
High	43 (20.2)	162 (23.3)	205 (22.6)	0.49[c]
Normal	170 (79.8)	532 (76.7)	702 (77.4)	

Abbreviations: IQR, interquartile range; ARV, antiretroviral.

[c] Chi-square statistical test was used to test for association.

[w] Wilcoxon rank sum test was used to test for median difference

*p-value highlighted in bold indicate the finding is statistically significant at α=0.05 (p< .05)

Table 1.3 Participants Characteristics stratified by Metabolic Syndrome

	Metabolic Syndrome		Total	P-value
	Yes	No		-
Demographics	**N (%) = 629 (29.2)**	**N (%) = 1522 (70.8)**	**2151**	
Age				
Median (IQR)	51.0 (41.0-61.0)	42.0 (30.0-54.0)	45.0 (33.0-57.0)	**<0.01** [w]
20-35	107 (17.0)	543 (35.7)	650 (30.2)	**<0.01**[c]
36-55	271 (43.1)	640 (42.0)	911 (42.4)	
>55	251 (39.9)	339 (22.3)	590 (27.4)	
Gender				<0.57
Female	332 (52.8)	783 (51.5)	1115 (51.8)	
Male	297 (47.2)	739 (48.5)	1036 (48.2)	
Race				**<0.01**[c]
Hispanic	175 (27.8)	331 (21.8)	506 (23.5)	
White	262 (41.7)	614 (40.3)	876 (40.7)	
African- American	124 (19.7)	314 (20.6)	438 (20.4)	
Other Race/Multi-racial	68 (10.8)	263 (17.3)	331 (15.4)	
Education				**<0.01**[c]
≤ High School	307 (48.9)	602 (39.6)	909 (42.3)	
> High School	321 (51.1)	919 (60.4)	1240 (57.7)	
Marital Status				**<0.01**[c]
Married	365 (58.0)	779 (51.2)	1144 (53.2)	
Others	264 (42.0)	743 (48.8)	1007 (46.8)	
Poverty to Income Ratio				
Median (IQR)	1.9 (1.0-3.6)	2.2 (1.0-4.5)	2.1 (1.0-4.2)	**0.01** [w]
<1.00	194 (30.8)	446 (29.3)	640 (29.8)	**<0.01** [C]
≥1.00-4.00	310 (49.3)	663 (43.6)	970 (45.2)	
>4.00	125 (19.9)	413 (27.1)	538 (25.0)	
Cigarette Use				**<0.01**[c]
Current Smoker	159 (25.3)	341 (22.4)	428 (24.0)	
Past Smoker	158 (25.1)	293 (19.3)	403 (22.5)	
Non-smoker	312 (49.6)	888 (58.3)	956 (53.5)	
Alcohol Use				**<0.02**[c]
Current Drinker	221 (24.1)	696 (75.9)	917 (100.0)	
Nondrinker	83 (31.4)	181 (68.6)	264 (100.0)	
Marijuana Use				**0.02**[c]
Current user	39 (17.7)	181 (82.3)	220 (100)	
Never user	188 (26.9)	512 (73.1)	700 (100)	
Concurrent Use				**0.02**[c]
Yes	21 (13.6)	134 (86.4)	155 (100.0)	
No	116 (26.4)	324 (73.6)	440 (100.0)	

Abbreviations: IQR, interquartile range; ARV, antiretroviral.

[c] Chi-square statistical test was used to test for association.

[w] Wilcoxon rank sum test was used to test for median difference

*p-value highlighted in bold indicate the finding is statistically significant at α=0.05 (p< .05)

Table 2.1: Summary of Stepwise Selection to identify predictors of metabolic syndrome with Alcohol Use as main independent variable

Step	Effect Entered	Effect Removed	DF	Number In	Score ChiSq	Pr > ChiSq
	Alcohol		1	5	2.40	0.12
	Age Group		1	1	54.49	<0.01
	Race		1	2	9.35	<0.01
	Education		1	3	3.93	0.05
	Marital status		1	4	2.69	0.10
	Cigarette smoking		1	6	2.60	0.16

Table 2.2: Summary of Stepwise Selection to identify predictors of metabolic syndrome with Marijuana Use as main independent variable

Step	Effect Entered	Effect Removed	DF	Number In	Score ChiSq	Pr > ChiSq
	Marijuana		1	6	2.87	0.09
	Age Group		1	1	35.9	<0.01
	Race		1	2	14.10	<0.01
	Poverty		1	3	2.52	0.11
	Marital status		1	4	2.41	0.12
	Cigarette smoking		1	5	1.18	0.28

Table 2.3: Summary of Stepwise Selection to identify predictors of metabolic syndrome with Concurrent Use as main independent variable

Step	Effect Entered	Effect Removed	DF	Number In	Score ChiSq	Pr > ChiSq
	Concurrent Use		1	3	2.98	0.08
	Age Group		1	1	31.06	<0.01
	Race		1	2	8.12	<0.01
	Cigarette smoking		1	4	2.21	0.14
	Poverty		1	5	1.09	0.30

Table 3.1: Unadjusted Odds ratio for metabolic Syndrome stratified by alcohol, marijuana, and concurrent use

Participant Characteristics	Crude OR (95% CI)
Alcohol Use	
Non-drinker[a]	1.00
Current drinker	0.69 (0.51, 0.94)
Current Drinking Level	
Non-drinker[a]	1.00
Low/Moderate drinker	0.70 (0.49, 0.99)
Heavy drinker	0.82 (0.53, 1.25)
Marijuana Use	
Never user[a]	1.00
Current user	0.59 (0.40, 0.86)
Concurrent Use	
No[a]	1.00
Yes	0.44 (0.26, 0.73)

Abbreviations: OR, Odds ratio; CI, confidence Interval

a; reference category for alcohol/marijuana/concurrent use/current drinking level

Table 3.2: Multivariable adjusted OR for metabolic Syndrome stratified by alcohol, marijuana, and concurrent use

Participant Characteristics	Adjusted OR (95%)*
Current drinker[a] (Model 1)	**0.69 (0.49, 0.99)**
Hispanic[b]	**1.53 (1.06, 2.21)**
African American	1.05 (0.72, 1.54)
Other/Multi-racial	0.77 (0.50, 1.20)
36-55 Years[c]	**2.57 (1.80, 3.68)**
>55 Years	**3.36 (2.26, 4.99)**
PIR (1.00 – 4.00)[d]	1.12 (0.79, 1.58)
PIR (> 4.00)	0.88 (0.57, 1.35)
Current smoker[e]	1.20 (0.82, 1.76)
Past smoker	**1.72 (1.19, 2.48)**
Married[f]	1.26 (0.93, 1.69)
≤High School[g]	1.18 (0.87, 1.76)
Current marijuana user[a] (Model 2)	0.62 (0.38, 1.01)
Hispanic[b]	1.11 (0.73, 1.67)
African American	0.82 (0.52, 1.30)
Other/Multi-racial	**0.48 (0.29, 0.80)**
36-55 Years[c]	**2.26 (1.55, 3.29)**
>55 Years	**3.65 (2.06, 6.45)**
PIR (1.00 – 4.00)[d]	0.96 (0.67, 1.38)
PIR (> 4.00)	0.68 (0.41, 1.12)
Current smoker[e]	1.53 (0.97, 2.43)
Past smoker	0.74 (0.42, 1.31)
Married[f]	1.27 (0.90, 1.80)
≤High School[g]	1.04 (0.73, 1.48)
Concurrent Use[a] (Model 3)	**0.53 (0.28, 0.99)****
Hispanic[b]	1.34 (0.79, 2.27)
African American	0.83 (0.47, 1.47)
Other/Multi-racial	0.64 (0.34, 12.0)
36-55 Years[c]	**2.95 (1.85, 4.68)**
>55 Years	**4.00 (1.98, 8.05)**
Current smoker[e]	1.50 (0.83, 2.72)
Past Smoker	0.93 (0.45, 1.94)
≤High School[g]	1.15 (0.75, 1.77)

Abbreviations: OR, Odds ratio; CI, confidence Interval; PIR, Family Income to Poverty Ratio

*Adjusted model for alcohol and marijuana use included the following covariates: Age, Race, Educational Level, Marital Status, Poverty, and Cigarette Smoking status.

**Adjusted model included the following covariates: Age, Race, Educational level, Cigarette smoking status.

a; reference category for alcohol/marijuana/concurrent use—nondrinker/never user/non-concurrent user,

b; reference category for race—Whites

c; reference category for age group—age group 20-35 years

d; reference category for family to income ratio—PIR < 1.00

e; reference category cigarette smoking—never smoker

f; reference category for marital status—others

g; reference category for level of education—> High school